Fecal microbiota transplantation for improved Fructose catabolism and Insulin sensiTivity In patients with metabolic syndrome : the FFIT study

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We would like to investigate if use of donor FMT enriched desulfovibrio bacterial strains has a beneficial effect on gut microbiota diversity and subsequent improvement of (diet derived) fructose catabolism and insulin sensitivity in patients with...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON49935

Source
ToetsingOnline

Brief title
FFIT study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
insulin resistance/Dm2, microbiota

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ZONMW NWO VICI grant

Intervention

Keyword: fructose catabolism, gutmicrobiota, insulin resistance, plasma metabolites

Outcome measures

Primary outcome

Primary outcomes are changes in periperhal insulin sensitivity(as determined by stable isotope (6-6-D2) based hyperinsulinemic clamp for calculation of endogenous hepatic glucose prodution). Also, changes in glucose excursions as detrmined by FreeStyle Libre sensors in relation to changes in (oral , small intestinal and fecal) gut microbiota diversity and composition at baseline and after 6 weeks of FMT.

Secondary outcome

Secondary endpoints are changes in post fructose (13c stable isotope) challenge enrichment of metabolites including alcohol in plasma, 24h urine , 24h feces as well as changes in small intestinal fructose receptor expression and fructose oxidation in exhaled air at these timepoints.Other secondary outcomes comprise changes in MRI imaging of hepatic fat content measured before and after FMT as well as changes in fecal and plasma SCFA and bileacid levels.

Study description

Background summary

The incidence and progression of insulin resistance to subsequent type 2 diabetes (DM2) is different between Surinamese-Hindoestani versus Caucusian .

metabolic syndrome patients in The Netherlands. Based on our previous research (Deschaschaux/Nieuwdorp, Nature Medicine 2018) we showed that altered catabolism of dietary fructose by diferent gut microbiota in these patients groups is associated with this different insulin resistance/DM2 progression and that desulfivibrio strains are important in maintaining gut microbiota diversity and stabitillity. .Previous research from our group has shown that donor fecal transplantation has beneficial effects on increasing gut microbiota diversity and subsequent insulin sensitivity in Caucasian metabolic syndrome subjects (MEC 07/114, 11/023 en 13/090)., however this is not known for Surinamese-asian metabolic syndrome subjects We thus expect that using donor fecal transplantations enriched in desulfovibrio strains will improve (dietary) fructose catabolism and insulin sensitivity (driven by improved gut microbiota diversity and plasma metabolites) in both surinamese asian and caucasian dutch metabolic syndrome subjects. An approach by which gutmicrobiota diversity and insulin sensitivity improvement is targeted by using a selected specific fecal donor has never been done before. We expect to find ethnicity specific involved gut microbial strains as well as (dietary fructose derived) plasma metabolites that are involved in insulin sensitivity in Surinamse-hindoestaan tversus Caucasian Dutch metabolic syndrome subjects. This could lead to new diagnostic and therapeutic (dietary) approaches based on personalized medicine to alleviate insulin resistance / Dm2 disparities in these different ethnic groups .

Study objective

We would like to investigate if use of donor FMT enriched desulfovibrio bacterial strains has a beneficial effect on gut microbiota diversity and subsequent improvement of (diet derived) fructose catabolism and insulin sensitivity in patients with metabolic syndrome from either Surinamese hindustani or caucasian douch descent. . By identifying which involved bacterial strains and their (from dietary fructose) produced plasma metabolites are associated with changes in glucose metabolism, we hope to pave the way for new personalized treatment (using either specific diet of cocktail of identified bacterial strains) to treat these specific patiënt groups against diabetes.

Study design

double blinded randomized controlled intervention trial

Intervention

donor fecestransplantaton (allogenic) or fecal transplantation with own feces (autologous)

Study burden and risks

2x gastroduodenoscopy (<0.01% chance of complications), hypersinulinemic clamp with energy expenditure (REE) as well as fructose test using stabiele isotopen (no complications in AMC in the last 20 years). fecal transplant using screened donor feces was also safe in the last 15 years when few hundred of these have been performed at AMC .use of freestyle libre sensor and MRI have not been associated with complications either. In conclusion, we feel that the new insight that we will gain by dissecting the role of specific gutmicrobiota strains and their produced metabolites on ethnic differences in insulin resistance/DM2 and the role of dietary fructose herein outweighs the risks and time investment of this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

patients:

-treatment naive metabolic syndrome/insulin resistant subjects
-surinamese asian or caucasian ethnicity
- male/postmenopauzal female
- age 40-65 years

donors:
-healthy (no medication use)
- enriched gutmicrobiota desulfovibrio levels

Exclusion criteria

-unable to provide written informed consent-
- antibiotics / PPI-antacids use in the last 3 months
- nicotine/alcohol abuse

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-02-2022
Enrollment:	56
Type:	Actual

Ethics review

Approved WMO

Date:	29-10-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL78355.018.21